THE NERVOUS MECHANISM OF RESPIRATION.

A LECTURE DELIVERED IN THE COURSE OF PHYSIOLOGY AT THE CHICAGO MEDICAL COLLEGE.*

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THE anatomical details of the nerves supplying the respiratory muscles have been fully pointed out to you on a previous occasion. We learned, at that time, that they all emerge from the spinal cord at different levels. The fine coördination of the various movements concerned in breathing leads us to suspect that the various nerves are all related to one governing centre. The exact position of this centre can be learned by a series of sections through the cerebro-spinal axis. These sections must begin above, since, were we to commence below, we would cut off from the upper part of the cord the different nerves which enter it below the point of section. We can destroy or remove the various parts of the brain without interfering with the normal breathing, until we proceed downward to the medulla oblongata. Any injury done to this part, however, will influence or even arrest the respiratory movements. Since the teachings of Floürens it has been customary to speak of a respiratory centre in the medulla oblongata. Its position is immediately above the lower end of the calamus scriptorius, extending upward as far as the alæ cinereæ.

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* The original lecture has been slightly condensed in some parts, so as to bring more into prominence the most recent additions to our knowledge.

Whenever this point is wounded, the breathing stops suddenly. Since the maintenance of life depends upon the continuance of breathing, the term "vital knot" was very properly chosen for this so-called respiratory centre. In fact, physiologists frequently resort to pricking the medulla with a stylet when it is desired to kill an animal very quickly. This alleged respiratory centre is really a double organ; it consists of two bilateral halves. A longitudinal section through this "vital knot," exactly in the median line, does not reveal itself in any disturbance of breathing. In other words, each half can act independently of the other, but as long as no other mutilation exists the two act in concert.

If, however, one or both pneumogastric nerves are divided, this harmony of the two sides of the body ceases, and the respiratory movements of the two sides of the chest and of the two halves of the diaphragm occur no longer synchronously.*

Since section of one vagus alone does not disturb the harmony of the two sides as long as the "vital knot" has not been bisected, we conclude that the normal coördination of the two sides is enforced by transverse nerve-fibres connecting the two halves of the respiratory centre.

But strangely enough there exists no anatomical basis for this alleged respiratory centre. At this spot, described above, no ganglionic cells are found to justify the term nerve-centre from an anatomical standpoint. Dissection reveals only bundles of nerve-fibres on either side of the median line, which fasciculi interchange fibres by decussation. These bundles can be traced from the origin of the cranial nerves arising in the medulla oblongata down into the cervical part of the spinal cord. They thus connect the nuclei of some of the cranial nerves, especially those of the vagus, with the origin of the motor nerves supplying the respiratory muscles. The real respiratory centre has lately been shown to be much larger in extent than the spot termed "vital knot."

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* Langendorff, *Centralbl. f. d. Med. Wissensch.*, 1879, No. 51.

Some observations made in Stricker's laboratory proved that after severing the cord from the medulla oblongata a few irregular respiratory movements could yet occur.* Especially was this the case on increasing the irritability of the spinal cord by means of strychnia. We have learned previously, in connection with the vaso-motor centres, that division of the spinal cord will place the lower end in a state of shock or temporary paralysis which, in mammals, requires days to recover from. A high division of the cord does not permit the animal to live long enough to recover, but an approach to the normal state can be produced by poisoning with small quantities of strychnia. Hence spinal centres may not reveal their existence after their separation from the higher centres, unless we exalt artificially their irritability.

This condition of shock owes its origin, at least in part, to the excitation of inhibitory fibres by the mechanical section. You will learn later about the existence of fibres coming from the brain downward, which, when active, diminish the irritability of the spinal cord below. This inhibitory system is imperfectly developed at birth. Hence, in very young animals, the spinal cord is not so much depressed by severing it from the medulla oblongata. In new-born cats and dogs Lautenbach succeeded in keeping up the respiratory movements after destruction of the medulla oblongata, at least for a number of minutes.†

By selecting new-born cats and rabbits for experiment, Langendorff‡ has recently succeeded in demonstrating the spinal respiratory centres in a more positive way. If, after the separation of the cord from the medulla, artificial respiration is practised for some time, the animal will resume a perfectly normal mode of breathing in a few minutes after stopping the bellows. The constancy of the result can be increased by poisoning with minute doses of strychnia. These breathing movements, governed as they are by isolated spinal centres, are perfectly normal in extent and co-ordination. Moreover, the activity of these spinal centres can be influenced in a reflex manner by stimulation of the sensory nerves, and the results are quite comparable to the reflex disturbances of breathing which can be so easily produced in the unmutilated animal. The exact extent of the spinal respiratory centres was not determined, but they probably exist as low as the origin of the last dorsal nerves, innervating the intercostal muscles. It is best, perhaps, to drop the idea of a discrete respiratory centre, and to suppose simply that the central ends of the different nerves concerned in respiration are more or less connected with each other by association-fibres. Moreover, the points of origin of the different nerves active in normal, undisturbed breathing, must possess equal degrees of irritability, since the same stimulus throws them alike into activity. Indeed, it can even be seen that in the severed head of a young animal the respiratory movements of the nostrils agree in rhythm with those of the trunk, although the former are innervated by the isolated medulla, and the latter by the separated spinal cord (Langendorff).

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* Rokitansky, *Wiener Med. Jahrbücher*, 1874, p. 30. Schroff, *Ibid*, 1875, p. 324.

† *Philadelphia Med Times*, 1878, May 11th, p. 366.

‡ *Arch. f.* (*Anat. &*) *Physiologie*, 1880, p. 518.

The next question must be, how do the impulses reaching the respiratory muscles, originate? We have seen so many instances of reflex action in the regulations of nutritive movements as to cause us to enquire whether breathing is also a reflex process. But this can be safely denied, although it may be difficult to disprove it by direct experiment. We can, of course, not cut off the respiratory centre from all sensory nerves. Any observations made on narcotized animals would likewise not be conclusive, since narcotic agents do not abolish all reflexes at one and the same time. Although breathing continues during ordinary narcosis, it will finally stop if the state of unconsciousness is pushed far enough.

The conclusive proof that breathing is not a reflex movement consists in the fact that we are acquainted with the stimulus creating the impulses in respiratory nerves, and that we know upon what organ this stimulus acts. This stimulus is the condition of the blood of the medulla oblongata, or, more properly speaking, in the respiratory centres. The activity of these centres is in exact proportion to the necessity for breathing as indicated by the arterial or venous nature of the blood sent to the centres. Whenever any impediment exists, interfering with the normal aeration of the blood, the breathing movements are exaggerated. They become both more frequent and more energetic, by reason of a larger number of muscles involved. The impediment may be of a mechanical nature, an obstacle to the passage of air into or from the lungs, or it may be an interference with the aeration of the blood, due to circulatory disturbances. The symptoms of dyspnœa or impeded breathing are the same, whether the cause is complete or partial closure of the trachea, or complete or partial obliteration of the pulmonary artery. In either case the blood is not sufficiently aerated, and the respiratory centre feels the call for a stronger ventilation, and responds to it by increased activity. We can demonstrate directly that it is only the condition of the blood in the nerve-centres which regulates the energy of breathing. If we close suddenly the four arteries supplying the brain and upper part of the cord, namely, the carotid and vertebral arteries on both sides, most intense dyspnœa is at once manifested. The energetic movements of the chest resulting therefrom certainly ventilate the lungs thoroughly. The aeration of the blood is likewise not prevented by any obstacle, but the respiratory centres do not receive any of this arterialized blood, and hence this artificially created condition leads to the same compensatory consequences which would follow the more ordinary interferences with aeration of the blood. We find here the same adaptation of the system to variable external conditions to be encountered in other branches of physiology. The greater the difficulty of getting air, the greater will be the effort to overcome the difficulty.

In the same manner as the respiratory centre responds by increased activity to an inadequate supply of arterial blood or to blood imperfectly arterialized, so it will, on the other hand, relax in its activity when it receives a due quantity of perfectly aerated blood. The reverse of dyspnœa or labored breathing is the state of apnœa. During this condition there occur no respiratory movements, because there is no need for them. Whenever the blood reaching the respiratory centres is perfectly arterialized, the activity of these centres ceases. In other words, the stimulation of the respiratory centre is due to want of oxygen in the blood. When the bellows are vigorously used, which are connected with the dog on the table, you will notice, first of all, that the spontaneous breathing ceases, the animal yields passively to the inflation, and no movements occur except those caused mechanically by our ventilation. The animal before us is narcotized, but the same results could have been obtained in a conscious dog.

After a vigorous use of the bellows, we will interrupt the artificial respiration suddenly. You can notice no breathing occurs during the space of nearly one minute. The breathing was not interfered with. It stopped simply because there was no need for it. The animal was in a state of apnœa. The blood was so perfectly arterialized by the energetic inflation as not to stimulate the respiratory centre at all.

We can perform the same experiment ourselves.

On stopping your breathing voluntarily, you will find it very difficult to maintain rest for a minute. The anguish due to the venosity of the blood compels you to resume breathing in spite of your will, but if you take a series of unusually quick and deep inspirations, you will find it easy to suspend breathing thereupon for a full minute or even longer. The blood is thereby so fully arterialized that considerable time is required before it becomes venous enough in character to stimulate the respiratory centres.

The maintenance of apnœa is not due merely to saturation of the arterial blood with oxygen, since even normally at least fifteen-sixteenths of the hæmoglobin in the arteries is combined with oxygen. But the energetic ventilation leading to apnœa necessarily renovates the residual air in the lungs more thoroughly, so as to leave a store of oxygenated air in the lungs from which the blood can draw its supply without the need of respiratory movements.*

The activity of the respiratory centres varies thus in an inverted ratio with the arterialization of the blood. The mechanism is self-regulating. The energy displayed is in proportion to the energy required to keep the blood arterialized. But how are we to explain the regular alternation of inspiratory and expiratory movements? What is the mechanism controlling the respiratory rhythm? Are we to look for separate inspiratory and expiratory centres? No satisfactory answer can yet be given to these questions.

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*Gad, Habilitätsvorlesung, Ueber Apnœa, etc. Würzburg, 1880.

Our insight into the central mechanism is but very incomplete.

Normally, the expiratory movement is almost wholly passive. You will remember that it is due mainly to the elasticity of the lungs and the chest-walls, the only muscles involved being the internal intercostal muscles. Hence, the supposition of a separate expiratory centre is hardly necessary. The central mechanism may consist simply in alternate discharge and rest of the inspiratory centre. Moreover, no expiratory movement can be directly produced by stimulating the nerve-centres. Lately, Kronecker and Marckwald have made the following experiments:* They severed the medulla oblongata from the pons in rabbits. The breathing is thereby not disturbed if the operation succeeds. On sending induction shocks through the medulla, inspiratory movements were produced, but no expiratory efforts. Whenever the stimulation coincided with an inspiratory movement, it enforced it; whenever the current passed through the centre during expiration, it arrested it. A point of special interest in these researches was the discovery that during complete apnœa the centre did not respond to electric stimulation.

But we must not lose sight of the fact, that during dyspnœa the expiratory movements are indeed active, and that muscular contractions resulting in expiration can be produced in a reflex manner to be described later on. No explanation of these occurrences can be given.

While the total energy of respiration depends on the state of the blood, the distribution of the energy is influenced vastly by impulses reaching the respiratory centres through different nerve-strands. We see but too often the effect of emotions on breathing. The movements are suspended for a time by terror, accelerated by exciting emo-

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***Arch. f. Phys.*, Heft 5 and 6, p. 592, 1880.

tions. The sigh of relief is but a deep and slow inspiration. Dread leads, on the other hand, to increased frequency of inspiration. It is quite likely that these and numerous similar instances are due to the influence of accessory respiratory centres recently discovered in the brain by Martin and Booker.* These observers learned that there exists a spot in the gray substance around the aquæduct of Sylvius, beneath the corpora quadrigemina, irritation of which increases the frequency of breathing. This effect is really due to exalted activity of the inspiratory muscles, which do not relax fully during the brief expiratory intervals. On increasing the stimulus, the action of the inspiratory muscles becomes tetanic at last, so that the chest is kept in the inspiratory position. On shifting the electric needles, the effect ceases. The authors claim also that an expiratory centre is to be found further back near the pons, which augments in the same manner the expiratory movements. These statements have been confirmed, apparently without knowledge of Martin and Booker's results, by Christiani.† You must not suppose, however, that these centres assist in ordinary respiration. As already stated, the breathing is not altered sensibly by removing the brain.

A most important influence upon the respiratory centre is exerted by the vagus nerve. This is evident at once on severing the nerve. Division of one nerve alone does not alter the breathing, unless the medullary "vital knot" has previously been bisected longitudinally, in which case the irregularity of breathing is confined to the muscles of the same side, while the other side moves with the normal rhythm. If both nerves are divided, the breathing becomes very slow. Our dog on the table breathes about 30 times a minute. Now, after having severed the pneumogastric nerves, the frequency has been reduced to 6 breaths a minute. You may notice that the retardation occurs during the inspiratory period. After a long pause, there begins a slow but very deep inspiration, sometimes persisting even as inspiratory tetanus. Suddenly it is interrupted by an expiration nearly normal, or, if anything, very sudden. Moreover, the breathing is irregular. Two successive respirations vary often appreciably in duration. But the total energy of respiration is not altered. What the inspirations lack in frequency they make up in depth. Voit has shown by actual test that the gaseous exchange of the animal is not reduced. But while the respiratory centre does enough work, the work is not distributed uniformly or advantageously. The centre lacks the regulation due to impulses sent from the lungs to the medulla through the pneumogastric nerve.

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* *Journal of Physiology*, vol. i, p. 370.

† *Centralblatt f. d. Med. Wiss.*, 1880, No. 15.

Breuer and Hering have shown that these regulating impulses originate in the lungs from mechanical causes. These observers claim that certain fibres of the vagi nerves are stimulated by expansion of the lungs, *i. e.*, by inspiration, and that these fibres check any further inspiratory movements, but favor expiration. They state further that other fibres in the same nerves are stimulated by the mechanical collapse of the lung tissue, and that these latter nerve-filaments, when active, excite a renewed inspiratory effort. The experiments upon which they base these conclusions are the following: If, in a tracheotomized animal, the lungs are inflated with bellows, and the tracheal tube be now closed to prevent collapse of the lungs, the first spontaneous movement occurring is always one of expiration, even though the lungs be but moderately distended. But if the artificial respiration be stopped during the collapsed state of the lungs, the animal follows every time with an inspiration. This regular alternation is not dependent upon any anatomical restraint. At the end of an ordinary inspiration we can easily make a voluntary stronger inspiratory effort, and we can likewise exaggerate in depth the ordinary expiratory movement. The capital point is, that the regularity ceases on section of both pneumogastric nerves. While in the normal animal we can predict with certainty the next respiratory movement, this is no longer possible after vagotomy.

The experiments were repeated some years ago, with imperfect result, by Guttman and Gad. But, as Gad* himself admits, the fault was in the mode of observation, and especially in the employment of chloral as a means of narcosis. The chloral simply prevents the influence of the vagus upon the centre. Recently, Langendorff† has confirmed fully Breuer and Hering's views by the application of graphic methods.

The existence of such a double set of fibres, one of which arrests the inspiratory action of the centre, the other the expiratory, can be demonstrated by electric stimulation of the vagus trunk, *i. e.*, its central end after section of the trunk. Nearly twenty years ago Rosenthal pointed out that the vagus nerve possessed a function antagonistic to that of one of its branches, viz.: the superior laryngeal nerve. Stimulation of the latter branch with a mild current leads to diminished frequency of breathing by cutting short the inspirations and prolonging the expiratory pauses. A strong current will arrest the chest altogether in the expiratory position. Stimulation of the vagus trunk, however, below the superior laryngeal branch, leads to the opposite result. According to Rosenthal, a feeble excitation will accelerate breathing by favoring the inspirations, while a stronger stimulus will throw the inspiratory muscles, and especially the diaphragm, into tetanus, and thus arrest the chest in inspiration, at least for a minute or so. Whether this peculiar property of the laryngeal nerve is called into action during ordinary breathing, we do not know. We are ignorant, likewise, of the manner in which the impulses checking inspiration originate in this nerve. The existence of this function, however, has been confirmed by all observers. But not so with the trunk of the vagus. Rosenthal* himself claimed recently, that stoppage during inspiration is the constant result of stimulation of the nerve with not too strong a current. This statement formerly met with much opposition.

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* *Archiv f. Physiologie*, 1880, p. 7.

† *Archiv f. Physiologie*, Supplement Band, 1879, p. 48.

Later researches by other observers show that the trunk of the vagus does, after all, contain fibres which arrest breathing during expiration. Burkart† claims that such fibres exist in the inferior laryngeal nerve, and hence also in the trunk of the vagus, but that these fibres act indirectly upon the respiratory centre through the intervention of the brain. Their effect is, hence, prevented by narcosis. Even more positive statements are made by Langendorff.‡ He was able to obtain either expiratory or inspiratory arrest of breathing by electric irritation of the nerve. It is not easy to predict which result will set in. But it seems that the fibres producing arrest in expiration are not so easily fatigued as the other set, so that after prolonged stimulation inhibition of inspiration is the more constant phenomenon. The latter result occurs invariably on irritating the divided nerve by means of glycerine.

A very suggestive mode of experimentation has lately been pursued by Kronecker and Marckwald.§ They severed the respiratory centres from their more important nerve-connections by dividing the medulla underneath the pons and cutting the two vagi. Under these circumstances the respiration is very irregular in rabbits. It was then learned that stimulation of the central end of the vagus could produce either expiration or inspiration according to the time the stimulus was applied. The inspiratory movement, however, could be more easily obtained. But if the medulla was divided so low as to check the natural breathing, or if the breathing had ceased on account of hemorrhage, a continuous faradization of the pneumogastric nerves restored the respiration.

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* *Archiv f. Physiologie*, Supplement Band, 1880, p. 34.

† *Pflüger's Archiv*, 1878, vol. xvi, p. 427.

‡ *Königsberger Phys. Mittheibungen*, 1878, p. 33, and *Centralblatt*, 1879, No. 21.

§ *Archiv f. Physiologie*, 1880, p. 441.

These various facts, important as they are, do not suffice for a theory of the nervous mechanism. We can only say that the activity of the centre depends on the state of the blood, and that the regularity of the movements are influenced by the vagi nerves. But for the alternation of the inspiratory and expiratory movements, we lack, as yet, a sufficient explanation.

Not only the vagus, but nearly all sensory nerves of the body can modify the breathing movements. Sudden changes in rhythm are produced by almost any strong or painful impression. As a rule, feeble stimulation of a sensory nerve will accelerate, while intense excitation checks the breathing (Langendorff). These same changes can be obtained even after severing the spinal cord from the medulla oblongata, providing the animal still breathes. In such instances in which the shock of the cord prevents the resumption of normal breathing, stimulation of sensory nerves will aid the centres in recommencing their activity. Indeed, in practice we avail ourselves of this susceptibility of the respiratory centres to sensory impressions. Stimulation of the skin by dashing on cold water or slapping with wet cloths, has aided in the recovery of many an asphyxiated individual. This artifice is of particular value in obstetric practice, when the child does not breathe at birth. Should such stimulation fail, the rational course would be to heighten the irritability of the respiratory centre by supplying it with arterialized blood by means of artificial stimulation. Quite recently, Goyard presented a note to the French Academy * regarding a successful method of resuscitation in the case of a still-born child. After two hours of vain endeavors with ordinary means, he plunged the child into a hot bath (45° to 50° C.), and witnessed the recovery, although the heart had stopped beating at birth.

A peculiar modification of breathing is produced by the action of heat on the sensory terminations in the skin. I refer to heat dyspnœa, commonly known as panting. It consists in an excessive frequency of respiration, the movements being, however, quite shallow. It is not a form of asphyxia, properly speaking, There exists no impediment to aeration of the blood. Although the dog may breathe 300 times a minute, its blood is in the usual state of arterialization. The frequency is due to the influence of other nerves upon the respiratory centre.

Panting does not occur to any extent in man, but readily so in animals that do not sweat. An animal devoid of sweat glands and covered with hair, like the dog, regulates its internal temperature largely by the dissipation of heat through the lungs. The more air passing through the lungs in a given time, the more heat will the animal lose in warming the inhaled air, and by evaporation from the lung surface. Hence, heat dyspnœa is a regulative provision of the economy in such animals, in order to guard against overwarming of the body. Panting is due to heating of the terminations of sensory nerves more than to overheated

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*Jan. 17, 1881. *L'Union Médicale*, No. 11, 1881.

blood. Still, Fick and Goldstein claimed to have produced it by warming the blood in the carotid arteries by means of hot tubes (50° C.) placed underneath the vessels. But their deductions have been contested by Sihler.*

It is doubtful whether their method really did warm the rapid blood-current to any extent, while the panting was actually due to the pain produced by the hot tubes. Yet it is fair to assume that the heat dyspnœa may be of central origin, since we witness it during the febrile state, even though the air is cool. Sihler, however, has shown that it is ordinarily caused by heating of the skin, and that it may occur even when but a small part of the skin is still connected with the respiratory centre, for instance, after section of the spinal cord in the cervical region.

Notwithstanding the excessive frequency of the movements during panting, the respiration is in reality not more efficient than ordinarily, on account of the shallowness of breathing. In some experiments which I have never published, I learned that the heat dyspnœa gives way at once to the much more vigorous though slower movements of true dyspnœa on closing the trachea of the animal, to return when the breathing was no longer impeded. On the other hand, the condition of apnœa can readily be induced during panting. On connecting the trachea with the bellows and ventilating the lungs thoroughly, I found that the animal remained motionless even in the hot chamber. The apnœa was of the usual duration, but was followed at once by the breathing characteristic of heat dyspnœa. We are to conclude, hence, that even in heat dyspnœa the condition of the blood is the ruling factor, regulating the energy of the respiratory centre.

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* *Journal of Physiology*, vol. ii, No. 3, p. 191; vol. iii, No. 1, p. 1.